

30. (New) The method of Claim 11, wherein the composition further comprises additional biologically-active factors admixed with or bound to the colloidal metal.

31.<sup>16</sup> (New) The method of Claim 15,<sup>11</sup> wherein the composition further comprises additional biologically-active factors admixed with or bound to the colloidal metal.

32. (New) The method of Claim 24, wherein the composition further comprises additional biologically-active factors admixed with or bound to the colloidal metal.

REMARKS

The present invention is directed to compositions comprising a colloidal metal, such as colloidal gold, and one or more biologically-active factors. The biologically-active factors may be admixed with the colloidal metal particles or may be bound to the colloidal metal particles. One or more of the biologically-active factors present in the composition of the invention may bind to a receptor on a cell membrane. The composition may also contain additional components such as excipients, buffers, antigen stabilizers, carriers, or adjuvants.

The present invention is also directed to methods for administering biologically-active factors to a human or animal by administering the compositions described above, including the targeted delivery of one or more biologically-active factors. Further, the present invention is directed to methods for vaccinating a human or animal and methods for treating cancer and immune diseases in humans and animals by administering the compositions described above.

With entry of the present amendment, Claims 1-32 are pending in the application. The claims have been amended to overcome the rejections under 35 U.S.C. § 112, and new claims 27-32 have been added. Support for these claims may be found throughout the specification and original claims. No new matter has been introduced by these amendments. The Commissioner is hereby authorized to charge Deposit Account No. 10-1215 in the amount of \$54.00 for the six additional dependent claims added by the present amendment. Also, it does not appear that the deposit account was charged for the \$249 fee due at filing for six additional claims in excess of twenty and five additional independent claims in excess of three. If, in fact,

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the deposit account has not been charged this amount, the Commissioner is hereby authorized to charge this amount to Deposit Account No. 10-1215.

Applicants appreciate the Examiner's reconsideration of the restriction requirement and examination of all of the claims. Applicant notes that the application has been filed with informal drawings. Formal drawings will be submitted upon indication that the application is allowed. Applicants appreciate the Examiner's indication that claims drawn to the treatment of cancer and immune diseases are allowable over the art.

The present amendment is accompanied by a petition for a one month extension of time and a check for \$55.00 to cover the fee for the one month extension of time. No additional fees, other than those listed above, are believed to be due with the filing of this amendment; however, the Commissioner is hereby authorized to credit overpayment, or charge any deficiency, to Deposit Account No. 10-1215.

**Rejection of Claims 1, 4, 9, 10, and 12 under 35 U.S.C. § 112, second paragraph**

Claims 1, 4, 9, 10, and 12 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the office action states that the "term 'admixture' in claims 1 and 9 is vague and indefinite because it is not clear how 'admixture' is the same as a conjugate or complex where the colloidal goal is **bound** to the biologically-active factor as exemplified in the specification." Applicants respectfully traverse this rejection for the following reasons.

The present invention comprises compositions which contain a combination of a colloidal metal and one or more biologically-active factors. The biologically-active factor may be admixed with the colloidal metal or may be bound to the colloidal metal. The specification discloses both compositions. For example, page 7, line 17, to page 8, line 13, discusses an admixture of a colloidal metal and a biologically-active factor, while page 8, line 14, to page 9, line 16, discusses preparations in which the biologically-active factors are bound to the colloidal metal particle. Additionally, note that the specification at page 16, line 2, to page 17, line 4, discusses a method for binding a biologically-active factor to the colloidal metal. In contrast,

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page 17, line 5, to page 18, line 5, of the specification discusses a process for admixing a biologically-active factor with the colloidal metal.

In some embodiments, it is preferable for the components of the composition to be admixed with one another. In other embodiments of the invention, it is preferable for the biologically-active factors to be bound to the colloidal metal. However, Applicants contend that it is clear from the specification how to form both the admixture and bound compositions and that it is also clear from the specification that the invention encompasses both embodiments. The claims have been amended to specifically recite compositions in which the biologically-active factors are either admixed with or bound to the colloidal metal. Therefore, Applicants assert that the use of the term "admixture" in the claims is not indefinite and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

The Office Action also states that claims 4, 10, and 12 are rejected because the term "the immunologically toxic biologically-active factor" lacks antecedent basis in the claims. Applicants have amended these claims to simply recite a "biologically-active factor." Therefore, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

**Rejection of Claims 1-3, 5, 6, 8, 9, 11, 13, 19, and 21 under 35 U.S.C. § 102(b) as anticipated by Shiosaka *et al.* (U.S. Patent No. 5, 112, 606)**

Claims 1-3, 5, 6, 8, 9, 11, 13, 19, and 21 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Shiosaka *et al.* The office action states that "Shiosaka discloses compositions comprising colloidal gold complexed with proteins and glucoproteins [sic] that may be administered to a mammal to induce an immune response." Applicants respectfully traverse this rejection for the following reasons.

Shiosaka *et al.* relates to a method for producing an antibody that is highly specific to a substance that is not antigenic unless it is bound to a carrier. Shiosaka *et al.* teaches that "it has been very difficult to provide an antiserum having a high specificity against substances of lower molecular weights, such as amino acids, low-molecular weight peptides and the like, because such substances have lower antigenicity or lower immune responsivities." Such substances provide little or no antibody production unless bound to a carrier in a hapten-carrier

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complex. Therefore, according to Shiosaka *et al.*, it is necessary to bind these substances to an appropriate carrier. The carrier chosen by Shiosaka *et al.* is colloidal metal.

In order for the substances described in Shiosaka *et al.* to produce antibodies, the substance must remain bound to the colloidal metal carrier, otherwise no useful antibody response will result. Independent Claims 1, 8, 9, 11, 19 and 21 have been amended to recite compositions and methods that require release of the biologically-active factors from the composition *in vivo*. Therefore, in contrast to the substances recited in Shiosaka *et al.*, the biologically-active factors of the present claims are released from the colloidal metal *in vivo*. Shiosaka *et al.* does not teach or suggest such *in vivo* release. In fact, Shiosaka *et al.* teaches away from the present invention by teaching the necessity of binding the antigenic substance to a carrier in order to provide for the production of antibodies. For these reasons, Applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

**Rejection of Claims 1-26 under 35 U.S.C. § 102(b) over WO 94/21288 ('288).**

Claims 1-26 have been rejected under 35 U.S.C. § 102(b) as being anticipated by WO 94/21288 ('288). The office actions states that "WO '288 discloses compositions and vaccines comprising colloidal metal, such as gold, chloride or silver, in combination with a biologically-active factor such as TNF- $\alpha$ . Said compositions/vaccines further include pharmaceutically acceptable carriers and Freund's complete adjuvant, respectively. Additionally, said compositions may [be] used to treat individuals suffering from cancer or immune related diseases. The vaccines may also be administered to a mammal to vaccinate said mammal against a normally toxic biologically-active factor. Preferred routes of administration are intramuscular and intravenous and the compositions may be administered singly or in multiple doses." Additionally, the Office Action states that "claims 19 and 21 are anticipated by WO '288 because WO '288 discloses administration of the same composition to a host using the method steps claimed by applicant. Accordingly, targeted delivery of the biologically-active factor is inherent."

The publication date of WO '288 is September 29, 1994. Applicants hereby claim priority as a continuation-in-part to application Serial No. 08/795,962, filed February 6,

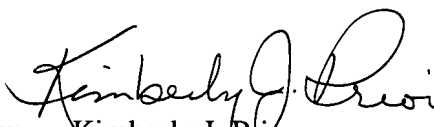
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1997, now abandoned, which is a continuation of application Serial No. 08/586,427, filed January 16, 1996, now abandoned, which is a continuation of application Serial No. 08/215,030, filed March 18, 1994, now abandoned, which is a continuation-in-part of application Serial No. 08/033,385, filed March 18, 1993, now abandoned. All of the subject matter of the present claims are supported by the parent application as originally filed. Thus, WO '288 is not prior art against the present application as its publication date of September 29, 1994, is later than the effective filing date, March 18, 1993, of the present application.

In light of the amendments and the above remarks, Applicants believe that Claims 1-26 are allowable over the prior art of record. Early and favorable consideration by the Examiner is solicited. If the Examiner believes any informalities remain in the application which may be corrected by Examiner's Amendment, or there are any other issues which can be resolved by telephone interview, a telephone call to the undersigned attorney at (404) 818-3700 is respectfully solicited.

Respectfully submitted,  
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